

REMARKS

Claims 1- 55 are pending in this application. Claims 3-7 and 13-50 have been withdrawn. Claim 53 has been cancelled. Claims 1, 51, 52 and 54 are amended.

Summary of Telephonic Interview

In the telephonic interview, Zhaoyang Li and Examiners Ford and Smith discussed the rejections in the Office Action and agreed to the following:

(1) Zhaoyang Li pointed out that the rejection of claims 1, 2, 8-12, 51-52 and 54 as indefinite can be overcome by replacing the phrase “a method for an agent” recited in the claims with the phrase “a method for screening for an agent” as Examiner Ford suggested. Regardless of the rejections against claims 52 and 54, claims 1, 2, 8-12 and 51 would be allowable;

(2) Examiner Ford clarified that the rejection of claim 51 as indefinite can be overcome by providing support for the phrase “endogenous to the fetal calvarial culture” in the specification. Zhaoyang Li indicated the Applicant will either amend the claims or indicate the support for the phrase in the specification.

(3) Regarding the rejection of claims 52 and 54 as lacking enablement, Zhaoyang Li maintained that claims 52 and 54 are enabled. In particular, Zhaoyang Li pointed out that U.S. patent law does not require the specification to provide what is well known in the art and in fact prefers the specification to omit information well known in the art so as to make the specification “clear and concise.” Zhaoyang Li further pointed out that while a stem cell or a bone marrow cell may differentiate into cells other than osteogenic cells, the conditions to guide a stem cell or a bone marrow cell to differentiate into an osteogenic cell has been well documented in the art.

Examiner Smith and Examiner Ford indicated that claims 52 and 54 will be re-examined if Applicant files a response within two months after the mailing date of the final office action. The Examiners asked Applicant to provide a short summary of the invention to aid them to examine claims 52 and 54.

Rejection under 35 U.S.C. 112, first paragraph

Claims 52 and 54 has been rejected as lacking enablement under 35 U.S.C. 112, first paragraph.

Summary of the Invention

Applicant of the present invention discovered NELL-1 peptide and found that this peptide is related to bone formation and that the bone formation process in an animal can be modulated by modulating NELL-1. Surrounding this discovery, in one aspect, the present application provides for (1) a method of screening for an agent that modulates bone mineralization in an osteogenic cell, (2) a method for screening for an agent that modulates NELL-1 gene or NELL-1 peptide, (3) a method for increasing bone mineralization, (4) a method for facilitating bone repair, and (5) a bone graft material capable of enhancing the formation of osseous tissue in an animal. Some examples of an osteogenic cell are, but are not limited to, an osteoblast, a mesenchymal cell, a fibroblast cell, a dura cell, a chondrocyte, a MC3T3 cell, a chondroblast, a stem cell, and a bone marrow cell.

Enablement of claims 52 and 54

The Examiner maintained that claims 52 and 54 lack enablement on the basis that a stem cell or a bone marrow cell may not necessarily differentiate into an osteogenic cell because a stem cell or bone marrow cell can differentiate into cells other than an osteogenic cell. Applicant agrees that a stem cell or a bone marrow cell can differentiate into cells other than an osteogenic

cell. However, Applicant points out that one of ordinary skill in the art would recognize that a stem cell or a bone marrow cell can differentiate into an osteogenic cell. Further, Applicant points out that the conditions for inducing a stem cell or a bone marrow cell to differentiate into an osteogenic cell have been well documented in the art. **For example, a simple search in PubMed on the differentiation of a stem cell or a bone marrow cell into an osteogenic cell uncovers hundreds of references on this topic.** Some examples of references on this topic includes Bianco, P., et al., "Multipotential cells in the bone marrow stroma: regulation in the context of organ physiology," Crit Rev Eukaryot Gene Expr. 9(2):159-73 (1999) (Review); Nordstrom, E., et al., "Osteogenic differentiation of cultured marrow stromal stem cells on surface of microporous hydroxyapatite based mica composite and macroporous synthetic hydroxyapatite," Biomed Mater Eng. 9(1):21-6 (1999); Sakai, A., et al., "Bone marrow cell development and trabecular bone dynamics after ovariectomy in ddy mice," Bone. 1998 Nov;23(5):443-51; Joyner, C.J., et al., "Identification and enrichment of human osteoprogenitor cells by using differentiation stage-specific monoclonal antibodies," Bone. 21(1):1-6 (1997); Krebsbach, P.H., et al., "Bone formation in vivo: comparison of osteogenesis by transplanted mouse and human marrow stromal fibroblasts," Transplantation 63(8):1059-69 (1997); Jaiswal, N., et al., "Osteogenic differentiation of purified, culture-expanded human mesenchymal stem cells in vitro," J Cell Biochem. 64(2):295-312 (1997).

Therefore, one of ordinary skill in the art can clearly see from the above examples of references, **while a stem cell or a bone marrow cell can differentiate into cells other than an osteogenic cell, inducing a stem cell or a bone marrow cell to differentiate into an osteogenic cell is well known in the art to one of ordinary skill in the art.** This is the part of the background knowledge that, according to the U.S. patent law, the applicant does not have to

provide, and preferably should omit, in the specification (see, In re Buchner, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co., 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984); see also MPEP §2164.01)). Accordingly, claims 52 and 54 are fully enabled to one of ordinary skill in the art and are patentably allowable. **If the Examiner still believes claims 52 and 54 lack enablement, Applicant respectfully invites the Examiner to explain what legal or factual basis justifies the Examiner's deviation from the settled rulings of court.**

Rejection under 35 U.S.C. 112, second paragraph

Claim 51 has been rejected as indefinite in that the phrase “wherein the osteogenic cell is a cell endogenous to a fetal calvarial cell culture” is allegedly unclear. Claim 51 is amended recite “wherein the osteogenic cell is a cell in a fetal calvarial cell culture.” Support is found in paragraphs [0179] to [0183], Example 1. Claim 51 is therefore clear and definite.


Claims 1-2, 8-12, 51-52 and 54 have been rejected as indefinite for reciting “a method for an agent that modulates...” The claims are amended to recite “a method for screening for an agent that modulates...” as the Examiner suggested. Claims 1-2, 8-12, 51-52 and 54 are not clear and definite. Therefore, regardless of the examination of claims 52 and 54, claims 1-2, 8-12 and 51 are now allowable.

CONCLUSIONS

Applicant respectfully points out that the examination of the present application has taken more than six years and has caused substantial financial burden on the Applicant. Applicant respectfully requests the prompt examination and will greatly appreciate the allowance of all the claims. **If the Examiner has any suggestions or amendments to the claims to place the claims in condition for allowance, applicant would prefer a telephone call to Zhaoyang Li for approval of an Examiner's amendment.** If the Examiner has any questions or concerns, the Examiner is invited to telephone the undersigned attorney at (415) 393-9885.

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Respectfully submitted,



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